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Liquid Collagen Wound Coverings Award Number N00014-90-J1797 Quarterly Report

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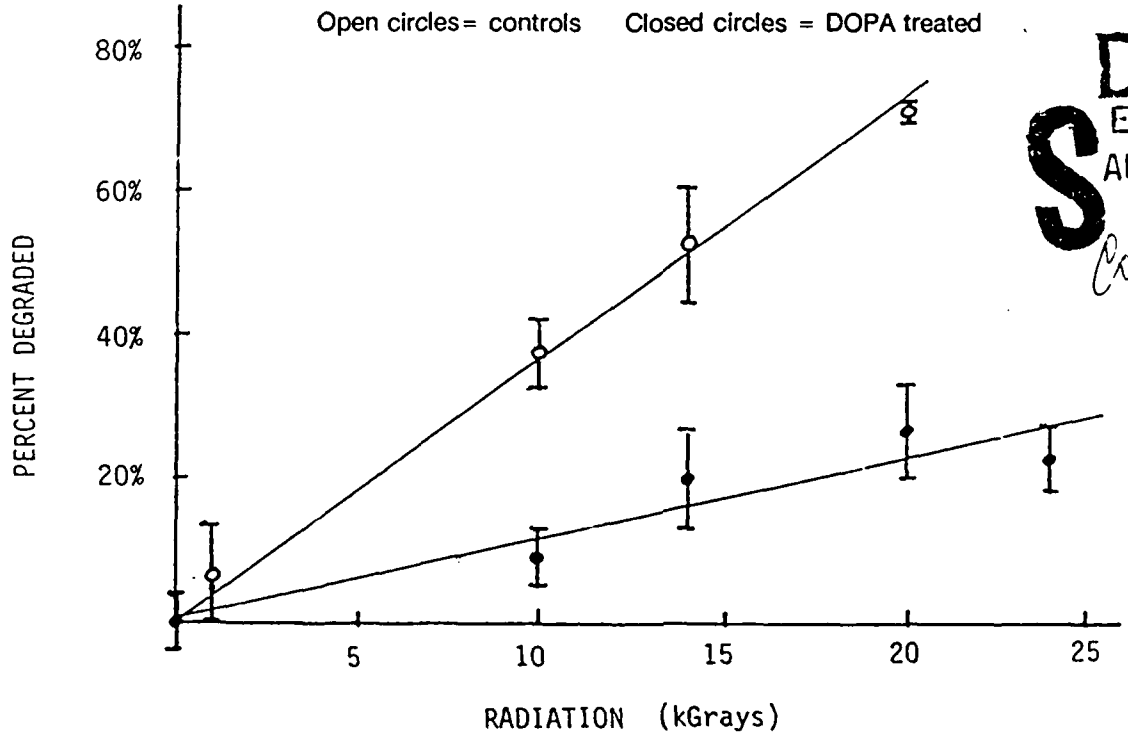
Human Studies

We have been fortunate to secure the services of a full time clinician whose major responsibility will be to enroll patients in the experimental protocol. Kathleen Waldorf, MD, will be hired as a Fellow in the Division of Plastic Surgery, August 1, 1990. Her goal is to enroll at least 20 patients into the study during the first six month period and study the outcome of application of the collagen dressings to the three wound types currently approved by the University's Human Subjects Committee.

Radioprotection by DOPA

The sterilization of proteins and protheses made of proteinaceous material is difficult. One attractive procedure is to subject the material to ionizing radiation (gamma rays), but this has been shown to degrade the protein. We have found that the addition of DOPA to collagen solutions immediately prior to lyophilization provides a dramatic protection from degradation. The figure below shows that a dose of 14 kGrays results in the degradation of 55 percent of the control collagen, but only about 16 percent of the DOPA containing collagen. Measured amounts of a bacterial culture (E. coli) were added to the collagen preparations prior to irradiation and bacterial survival was measured. Although there was a modest protection provided to the bacteria in the DOPA containing preparations, no bacteria survived dose levels of 1 kGray, a dose level which produced minimal degradation of the proteins.



Animal Studies

We have adapted a recently described animal wound model to this project. A one centimeter diameter plug of skin is removed from the inner surface of the rabbit ear and allowed to heal either with or without our collagen wound dressings containing growth factors. Because the skin is removed down to cartilage and there is no muscle underlying the skin, this type of wound heals only by the formation of granulation tissue and by epidermal covering. Wound contraction is not a factor and, because very standardized wounds can be made, numerical values regarding the rate of healing of the wound can be achieved. For example, the relative area covered by epidermis can be measured and the depth of invading granulation tissue can be measured on histological preparations. This model has great applicability to the study and is currently being used to determine whether, in fact, the Iodocoll preparations slow the rate of healing significantly.

Iodine and Collagen Gelling

This has been described in earlier progress reports. In short, the release of iodine into a solution of collagen brings about a rapid gelling and this we propose to use in a type of wound healing kit. An application for the issuance of a patent will be filed within the month.

Covalent Binding of DOPA

An individual has been assigned full time to study the conditions by which EDAC can activate the carboxyl groups on collagen or on DOPA so that amide bonds can form with free amino groups on the other component. Preliminary experiments show that this can be done and that DOPA is in fact bound to the collagen. We are currently in the process of 1) quantifying the binding, 2) studying optimum conditions for this binding, 3) determining the ability to resolubilize collagen which has had such DOPA bound to it.